Remarks

Amendments to the Claims

Claims 1-3 and 25 are amended to recite "human" NPFF2. The specification supports this amendment, for example, at page 1, line 9: "[T]he present invention relates to nucleic acid sequences and amino acid sequences of a human NPFF2 . . . ."

Claims 1-3 also are amended to recite that the contacting step occurs *in vitro*. The specification supports this amendment, for example, at page 39, line 10 to page 40, line 7, which describes later combining initial screening assays of the invention with *in vivo* assays.

Claims 1-3 are also amended to recite an identifying step. The specification supports this amendment on page 39, lines 13-16: "The methods entail the identification of candidate or test compounds or agents . . . which bind to NPFF2 and/or have a stimulatory or inhibitory effect on the biological activity of NPFF2 or its expression and then determining which of these compounds have an effect on symptoms or diseases regarding the hematological . . . diseases . . . ."

The amendment of claims 1-3 to recite agents "that may be useful . . . ." is inherent in the nature of a screening assay.

Claims 2 and 3 are amended to recite wherein the activity of the polypeptide results in an alteration of intracellular calcium. The specification supports this amendment on page 41, lines 15-16: "Among measures of activity are: alteration in intracellular Ca^{2+} concentration . . . ."

New claims 27-30 are supported by claims 4 and 6 as originally filed.

The amendments add no new matter.

Objection to Claims 1-3

Claims 1-3 are objected to because the word "and" was not placed between the method steps. Claims 1-3 are amended to insert the word "and" between the last two recited method steps.

Claim 3 is objected to because the phrase "at the presence of a compound" is awkward. Amended claim 3 recites "in the presence of a compound."

Please withdraw the objections.

Rejection of Claims 1-11 and 25 Under 35 U.S.C. § 112 ¶ 1 (written description)

Claims 1-11 and 25 stand rejected under 35 U.S.C. § 112 ¶ 1 as failing to comply with the written description requirement. The Office Action asserts that the specification only describes "methods of screening comprising use of a polypeptide of SEQ ID NO:2 (or residues 103-552 of SEQ ID NO:2 as taught by the prior art) . . . ." Applicants respectfully traverse the rejection.

Independent claims 1-3 as amended recite human NPFF2 polypeptides. Human NPFF2 was well known in the art before the priority date of this application. See page 4, lines 13-18 of the specification. The Court of Appeals for the Federal Circuit has held that an adequate written description of a gene which is well known in the art does not require a structural recitation either in the specification or in the claims. *See Capon v. Eshhar*, 418 F.3d 1349, 1360-61, 76 U.S.P.Q.2d 1078, 1087 (Fed. Cir. 2005) ("the Board erred in ruling that § 112 imposes a *per se* rule requiring recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field."). Applying the same logic, a sequence identifier for a well-known protein such as NPFF2 should also not be required.

According to *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316, 1327, 63 U.S.P.Q.2d 1609, 1615 (Fed. Cir. July 15, 2002), "the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed." One of skill in the art would readily recognize the genus of human NPFF2 polypeptides because these polypeptides were known in the art. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-11 and 25 Under 35 U.S.C. § 112 ¶ 1 (enablement)

Claims 1-11 and 25 stand rejected under 35 U.S.C. § 112 ¶ 1 as not being enabled for their full scope. Applicants respectfully traverse the rejection.

"The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988). The present specification meets this standard.

To advance prosecution several amendments have been made to independent claims 1, 2, and 3 to address points raised in the Office Action. The claims have been limited to *in vitro* methods, the use of human NPFF2 polypeptides, and (for claims 2 and 3), altered calcium mobilization as the NPFF2 activity. These amendments address the Office Action's assertions with respect to enablement of *in vivo* methods, the genus of NPFF2 polypeptides, and the modulation of other activities of NPFF2.

The Office Action makes several other arguments why claims 1-11 and 25 allegedly are not enabled. First, the Office Action asserts that "[n]either the specification nor the prior art teach [or] provide any reasonable correlation between NPFF2 activity and a hematological

disease." Office Action at page 6, lines 19-20. Applicants' invention is based on an association between NPFF2 activity and hematological diseases. Applicants agree that there is no evidence of record that this subject matter is taught in the prior art (see Applicants' rebuttal to the anticipation rejections below). The specification, however, does teach the association of NPFF2 with hematological diseases (page 58, lines 14-15) and supports this teaching with NPFF2 expression data from hematological tissues (Table 1).

Second, the Office Action asserts that the claims "encompass methods to identify therapeutic agents for any type of 'hematological disease,'" which it asserts is too broad. Bonini (cited in the rejection under 35 U.S.C. § 102(b), addressed below) teaches that the human NPFF2 receptor activates intracellular calcium mobilization in COS-2 cells expressing the recombinant receptors. See Figure 5 of Bonini. Miller[1] teaches that "elevation in [Ca_c] is an intracellular signal that mediates the effect of . . . hematopoietic growth factors." Miller at page 313, left hand column, lines 14-15. Miller also teaches that "[t]he proliferation and differentiation of hematopoietic cells are dependent on the presence of hematopoietic growth factors." Miller at page 309, lines 26-27. The specification teaches that the NPFF2 polypeptide is highly expressed in tissues of the hematological system. Specification at page 58, lines 13-15. Once the skilled artisan is provided with the teachings of the specification, a connection between NPFF2 and the genus of hematological diseases would be apparent.

Third, with respect to independent claim 1, the Office Action asserts that "[t]he fact that a test compound to bind [sic; binds] to an NPFF2 polypeptide does not allow the skilled artisan [to] predict whether or not said binding partner can also alter an activity of the NPFF2 polypeptide." Office Action at page 11, lines 13-15. The Office Action further asserts that "[a]

[1] Miller *et al.*, *J. Clin. Invest. 82*, 309-315, 1988, provided with the accompanying IDS.

test compound can bind to a receptor without alter its activity." Office Action at page 11, line 15. Claim 1 is simply a screening method for compounds which bind to a human NPFF2 polypeptide. Claim 1 does not require identification of a test compound which binds to a human NPFF2 polypeptide as also able to alter NPFF2 activity.

Fourth, the Office Action urges that "the skilled artisan would not be able to predict whether or not a modulator of the calcium mobilization produced by an NPFF2 polypeptide could be used to treat a hematological disease." Office Action at page 6, lines 17-19. Again, the claims are directed to screening methods. It is well known that not all agents identified in a screening method will become therapeutics, and the claims do not require confirmation that a test compound identified as a modulator of the calcium mobilization produced by an NPFF2 polypeptide can be used to treat a hematological disease.

Finally, the Office Action asserts that "[t]here are no examples that connect NPFF2 activity with any hematological disease." Office Action at page 4, lines 22-23. It is well settled, however, that working examples are not required to enable an invention. *In re Long*, 368 F.2d 892, 895, 151 U.S.P.Q. 640, 642 (C.C.P.A. 1966). The lack of a working example, therefore, should not be given undue weight because the inventors have provided adequate direction for carrying out the claimed methods.

The Examiner has the initial burden to establish a reasonable basis to question the enablement provided in the specification. *In re Wright*, 999 F.2d 1557, 1562, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993). The Office Action does not provide a reasonable basis to question the enablement of claims 1-11 and 25. Please withdraw the rejection.

Rejection of Claim 5 Under 35 U.S.C. §112, Second Paragraph

Claim 5 stands rejected as indefinite under 35 U.S.C. § 112 ¶ 2. Claim 5 has been canceled as redundant in light of the recitation "*in vitro*" in claim 1.

Rejections Under 35 U.S.C. § 102(b)

The Office Action contains two rejections under 35 U.S.C. § 102(b):

- claims 1, 4, 5, and 8 over Cikos;[2] and
- claims 1-11 over Bonini.[3]

Applicants respectfully traverse the rejections.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the claimed invention. *Richardson v. Suzuki Motor Co.,* 868 F.2d 1226, 1236 (Fed. Cir. 1989). Neither Cikos nor Bonini meets this standard.

The Office Action asserts that "Cikos et al teach a method of contacting a test compound (YY) with a NPFF2 polypeptide (NPGPR) and detecting binding of said test compound to said NPFF2 polypeptide . . . ." Office Action at page 16, lines 26-28. The Office Action asserts that " . . . Bonini et al teach a method of contacting a test compound ([I^{125}]1DMeNPFF) with a NPFF2 polypeptide and detecting binding of said test compound to said NPFF2 polypeptide." Office Action at page 18, lines 5-7. The Office Action further asserts that Bonini's Figure 5B

[2] Cikos *et al.*, *Biochem. Biophys. Res. Commun. 256*, 352-56, 1999.

[3] Bonini *et al.*, *J. Biol. Chem. 275*, 39324-31, 2000.

"shows a comparison of the activity of NPFF2 at various concentrations of the test compound NPFF." Office Action at page 18, lines 16-17.

Amended claim 1 recites an identifying step where a test compound is identified as an agent that may be useful in the treatment of a hematological disease if binding of the test compound to the human NPFF2 polypeptide is detected. Neither Cikos nor Bonini teaches any association of human NPFF2 with hematological disease. Thus, Cikos does not teach every element of independent claim 1, and Bonini does not teach every element of independent claims 1-3.

Applicants respectfully request withdrawal of the rejections.

Respectfully submitted,

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